

Amendments to the Drawings:

Enclosed herewith is an amended version of Figures 1A-13, in which the margins, lines, numbers, letters and characters are in compliance with 37 C.F.R. § 1.121(d). In accordance with the Office's revised format, these drawings have been labeled "Replacement Sheet."

REMARKS

Claims 1-47 were pending on the mailing date of the outstanding Office Action. Claims 17, 20, 25, 33 and 40 have been amended to include the subject matter of claims that were held to be allowable. Claims 30, 37 and 45 have been cancelled from the application. Therefore, claims 1-29, 31-36, 38-44, 46 and 47 are presently pending in this application.

The applicant would like to thank the Examiner for finding claims 17, 18, 20-24, 30-32, 37-39 and 45-47 to be allowable if rewritten in independent form. The status of the drawings, specification and other claims in the application in light of the Office Action dated 16 March 2006 is as follows:

(A) Corrected drawings in compliance with 37 C.F.R. § 1.121(d) were requested;

(B) Claims 1, 5, 25, 33 and 40 were rejected under the nonstatutory doctrine of obviousness-type double patenting;

(C) Claim 14 was rejected under 35 U.S.C. § 112, first paragraph; and

(D) Claims 1-4, 6-13, 15, 16, 19, 25-29, 33-36 and 40-44 were rejected under 35 U.S.C. § 103 over U.S. Patent No. 5,921,940 issued to Verrier et al. ("Verrier") and U.S. Patent No. 5,555,888 issued to Brewer et al. ("Brewer").

A. **Response to Request for Corrected Drawings**

The Examiner indicated that the margins in Figure 1B were not acceptable, and that the lines, numbers, letters and characters should be checked in other Figures. The drawings filed with the application were informal drawings, and the applicant has now obtained formal drawings. Accordingly, enclosed with this paper are replacement sheets for Figures 1A-13 in which the margins, lines, numbers, letters and characters comply with 37 C.F.R. § 1.121(d). The applicant respectfully submits that the formal drawings submitted with this paper comply with the Examiner's request.

B. Response to Obviousness-Type Double Patenting Rejection

Claims 1, 5, 25, 33 and 40 were provisionally rejected under the nonstatutory doctrine of obviousness-type double patenting over the following: claims 1 and 10 of U.S. Application No. 10/816,549; claim 22 of U.S. Application No. 10/815,290; and claims 1, 2 and 23 of U.S. Application No. 10/816,561. Claims 25, 33 and 40 have been amended to include the subject matter of allowable claims 30, 37 and 45. As such, the applicant respectfully requests withdrawal of the rejection of claims 25, 33 and 40 on the grounds that these claims are not obvious over the cited claims of the copending applications.

With respect to claims 1 and 5, the applicant does not concede to the merits of this rejection. Nonetheless, to expedite prosecution of the application, Terminal Disclaimers regarding U.S. Patent Application Nos. 10/816,549, 10/815,290, and 10/816,561 are enclosed with this response. The applicant respectfully reserves the right to withdraw these Terminal Disclaimers pending further prosecution of this application. In light of the Terminal Disclaimers, the applicant respectfully requests withdrawal of the obviousness-type double patenting rejection of claims 1 and 5.

C. Response to Section 112 Rejection

Claim 14 was rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the phrase "reducing the number of data points by a factor of between 5 and 30" is not enabled. The applicant respectfully disagrees with the Examiner because the claims constitute part of the disclosure, and claim 14 itself clearly discloses that smoothing the estimated alternan signature comprises reducing the number of data points by a factor between 5 to 30. Moreover, a person skilled in the art would be able to practice the process of claim 14 without undue experimentation. Nonetheless, paragraph [0059] of the specification has been amended to include the subject matter verbatim to provide direct support. Because the subject matter was filed in original claim 14, this amendment to the specification does not add new matter to the application. Therefore, the applicant respectfully requests withdrawal of the rejection of claim 14 under Section 112.

D. Response to Section 103 Rejection

Claims 1-4, 6-13, 15, 16, 19, 25-29, 33-36 and 40-44 were rejected under 35 U.S.C. § 103 over the combination of Verrier and Brewer. Claims 26-29 depend from claim 25, which has been amended to include the allowable subject matter of claim 30. Similarly, claims 34-36 depend from claim 33, which has been amended to include the allowable subject matter of claim 37. Claims 41-44 depend from claim 40, which has been amended to include the allowable subject matter of claim 45. As a result, independent claims 25, 33 and 40 have been amended to include allowable subject matter such that this rejection is now moot with respect to claims 25-29, 33-36 and 40-44. The following remarks accordingly address the patentability of claims 1-4, 6-13, 15, 16 and 19 over the combination of Verrier and Brewer.

1. Claim 1 is Directed Toward a Method of Determining an Alternan Signature by, *Inter Alia*, Differencing Temporally Adjacent T-Wave Segments While Maintaining Consistent Alternan Polarity of the Difference

Claim 1 is directed toward a method for determining an alternan signature estimate obtained from a physiological signal having substantially repeating physiologic waveforms representative of a subject's heart activity. One embodiment of the method of claim 1 comprises identifying T-wave segments of the repeating physiological waveforms, and computing estimated alternan signatures between temporally adjacent T-wave segments by differencing the temporally adjacent T-wave segments while maintaining consistent alternan polarity of the difference. Claim 1 further includes smoothing the estimated alternan signatures to obtain smooth alternan estimates, and identifying a dataset from the smoothed alternan estimates that represents a final alternan signature estimate curve. Because the differencing procedure maintains the polarity, the smoothing procedure and final alternan signature estimate curve also maintain the polarity of the difference.

2. The Applied Art is Directed Toward Methods that Obtain the Absolute Magnitudes or the Squares of Differences in Physiological Signals Without Retaining the Polarity of the Differences

Verrier is directed toward tracking cardiac vulnerability by analyzing T-wave alternans. Verrier discloses that alternans can be estimated using complex

demodulation techniques, subtraction estimation techniques, least square estimation, auto-regressive estimation, or auto-regressive moving average estimation procedures. With respect to differencing adjacent heartbeats, Verrier teaches a subtraction method for dynamic estimation of alternans in which T-wave portions of an ECG signal are partitioned into time divisions such that the area between the ECG signal and the isoelectric base line is computed for each time division by summing the areas of all samples in the time division. Verrier further teaches that the subtraction method involves "subtracting the area of each time division (n) of an R-to-R interval from the area of the corresponding time division of a subsequent (n+1), or alternatively, a previous (n-1) R-to-R interval to form a new time series $Y(n)$ representing the magnitude of the alternans." Verrier goes on to state "[B]ecause this difference series $Y(n)$ may be positive or negative, the absolute value or magnitude of $Y(n)$ is used for the magnitude $A(n)$." In the case of differencing adjacent T-wave segments, Verrier accordingly teaches disassociating the polarity information in the ECG signal from the alternan values by using the absolute value or "magnitude" of the alternans. (See, e.g., Col. 16, lines 14-48.)

Brewer is directed toward a method and apparatus for continuously, automatically and adaptively facilitating the electrical activity of a patient's heart. One aspect of Brewer is to construct an electrical instability waveform as shown in Figure 12 and described in the text at column 22, line 54 through column 23, line 22. The left side of Figure 12 in Brewer illustrates the algebraic difference 254 between points of the first extracted R-wave (R_1) and corresponding points of the second extracted R-wave (R_2). Brewer then teaches that "a comparison waveform 256 between the two R-waves is defined as a point by point squaring of the algebraic difference 254 between them." Notably, even though the algebraic differences between the two R-waves shown by line 254 include polarity, Brewer teaches that the actual comparison waveform 256 stored in the computer's memory for further use in the process is the square of the algebraic differences shown in line 254. Because Brewer squares the algebraic differences, all of the values for the differences in the comparison waveform 256 are positive. In the case of differencing adjacent R-wave segments, therefore, Brewer actually teaches a

differencing process that disassociates the polarity information in the ECG signal from the values by using the square of the algebraic differences.

3. Claim 1 is Patentable Over the Combination of Verrier and Brewer Because This Combination of References Fails to Disclose or Suggest, *Inter Alia*, Computing Estimated Alternan Signatures Between Temporally Adjacent T-Wave Segments by Differencing the Temporally Adjacent T-Wave Segments While Maintaining Consistent Alternan Polarity of the Difference

Independent claim 1 is patentable over the combination of Verrier and Brewer under Section 103 because this combination of references fails to disclose or suggest several features of this claim. For example, if Verrier's differencing was modified according to the teachings in Brewer, then the difference of the temporally adjacent T-wave segments in Verrier would be squared to provide a comparison waveform as taught in Brewer. Such a comparison waveform, however, inherently has only positive values disassociated from the polarity of the differences. The combination of Verrier and Brewer accordingly fails to disclose or suggest at least the feature of computing estimated alternan signatures between temporally adjacent T-wave segments by differencing the temporally adjacent T-wave segments while maintaining consistent alternan polarity of the difference. Therefore, claim 1 is patentable over the combination of Verrier and Brewer under Section 103.

The applicant respectfully disagrees with the characterization of Brewer set forth in the Office Action. More specifically, the statement that Brewer "discloses differencing temporally adjacent pairs from the cardiac cycle while maintaining the polarity, as shown in figure 12" is incorrect. Brewer teaches differencing temporally adjacent pairs from the R-wave segments of the cardiac cycle to obtain a point-by-point squaring of the algebraic differences that inherently loses the polarity of the differences between the R-wave segments. As a result, the applicant respectfully submits that the characterization of Brewer set forth in the Office Action is incorrect.

Claim 1 is further patentable over the combination of Verrier and Brewer because Verrier teaches away from computing estimated alternan signatures that maintain consistent alternan polarity of the differences. Based on the applicant's

understanding, the estimation by subtraction method disclosed in Verrier for estimating the amplitude of alternations for each time series requires the absolute value or "magnitude" of the alternans. As such, assuming for the sake of argument that Brewer teaches maintaining the polarity of the differences between adjacent heart beats, Verrier's process requires the absolute value of such differences to disassociate the polarity from the evaluation of the T-wave alternans. Verrier accordingly teaches away from the proposed combination set forth in the Office Action. Therefore, claim 1 is further patentable over the combination of Verrier and Brewer.


In light of the foregoing, claim 1 is patentable over the combination of Verrier and Brewer under Section 103. Claims 2-4, 6-13, 15, 16 and 19 depend from original claim 1, and thus these claims are also patentable over Brewer as depending from a patentable independent claim and also because of the additional subject matter of these claims. Therefore, the applicant respectfully requests withdrawal of the rejection of claims 1-4, 6-13, 15, 16 and 19 over the combination of Verrier and Brewer under Section 103.

E. Conclusion

In view of the foregoing, the pending claims comply with 35 U.S.C. § 112 and are patentable over the cited art. The applicant accordingly requests reconsideration of the application and respectfully submits that the claims are in condition for allowance. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned representative at (206) 359-3258.

Respectfully submitted,
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